

PATENT

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

In re Application of:

van Oosterhout et al.

Serial No.: 09/668,555

Filed: September 22, 2000

For: METHODS AND MEANS FOR THE
TREATMENT OF IMMUNE RELATED
DISEASES

Examiner: Ron Schwadron, Ph.D.

Group Art Unit: 1644

Attorney Docket No.: 2183-4541US

CERTIFICATE OF MAILING

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Allen C. Turner

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Assistant Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450
Attention: Board of Patent Appeals and Interferences

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Continuing in the same vein (*i.e.*, interpretation of the "consisting essentially of" transition language), paragraph (11) A) of the Examiner's Answer argues:

"Appellant seems to be arguing that the 'basic and novel characteristic of the claimed invention' as disclosed in the specification is the use of antibody immunotoxins specific for the T-cell and NK-cell lineage. However this description is clearly erroneous because the specification, page 6, discloses use of antiCD5 antibody in the instant invention, wherein the art recognizes that said antibody reacts with B cells (see Scannon, Table 1 under CD5)." (Examiner's Answer, p. 7).

And further,

"CD7 is found on pluripoential hematopoietic stem cells. Thus, even the particular combination of antibody immunotoxins recited in the claim bind cells other than T cells or NK cells." (*Id.*).

As a first point, page 4 of appellants' Specification specifically recites that the invention "provides a pharmaceutical composition for eliminating or reducing the number of unwanted CD3 and/or CD7 positive cells" and that "[t]ypically these cells are T-cells or NK-cells or other cells playing a role in GVHD or allograft rejection."

Furthermore, as one of skill in the art would appreciate that even though an antibody reacts or binds with a cell, that fact does not mean that the particular antibody would be useful for delivering a toxin to the cell. As is known to those of skill in the art, not only must the antibody bind the cell, but it needs to be internalized for the toxin to take effect. As would be recognized by one of skill in the art, immunotoxins may bind their target cells in a high number, but may still not be effective if the antibodies are not internalized. In other words, reported “reactivity of an antibody” with a cell would not automatically be interpreted as meaning that the antibody is useful as for delivering an immunotoxin to that cell.

Furthermore, with regard to the antiCD5-immunotoxin argument, Scannon et al. presents the CD5 antigen as: “one of the ‘pan T’ antigens, present on 85-100% of human mature T lymphocytes, and on a small population of B lymphocytes (page 14)”. Although one of skill in the art might consider antiCD5 antibody-immunotoxins as being potentially useful for eliminating T cells, with, as possible collateral damage, the eradication of a “small population of B lymphocytes”, an antiCD5 antibody immunotoxin would not be considered useful by one of skill in the art for the *in vivo* elimination of B cell lineage.

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Thus, the “basic and novel characteristic of the claimed invention” remains the same, *i.e.*, the treatment of immune related disease through the elimination of cells in the T-cell and NK-cell lineages and Scannon et al. does not disclose or teach such, particularly using the chosen antibodies.

In paragraph (11)B) of the Examiner's Answer, great weight is put on the later statement of one of the inventors that, "it is impossible from the clinical data to determine the exact contribution of SPV-T3A-DGA and WT1-DGA (or their MoAb moieties) to the observed biologic and clinical responses."

Appellants would respectfully point out that the mere observation that biological and clinical responses have been observed in the absence of any severe acute toxicities can be qualified as highly surprising. These clinical data indicated a clear therapeutic window where, in contrast, hardly one existed for other ricin A-based antibody immunotoxins tested. The definition of "synergism", being the interaction of two or more agents so that their combined effect is greater than the sum of their individual effects, by no means contradicts the statement that it is impossible to determine the exact contribution of the individual components to that combined effect. The *in vitro* experiments described in the same article clearly demonstrated several mechanisms of action, which one skill in the art knows to be relevant for *in vivo* efficacy: synergistic toxin-induced cell kill of T cells, activation induced cell kill of activated T cells, antigen modulation of CD3/TCR, toxin-induced cell kill of NK cells.

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Respectfully submitted,



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